

AMENDMENTS TO THE CLAIMS

1-2. (canceled)

3. (currently amended) A peptide according to ~~claim 1~~ claim 13 having the formula:

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH₂, or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH₂; or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH₂.

4. (canceled)

5. (currently amended) A CRF cyclic peptide according to ~~claim 1~~ claim 15 having the formula:

Y₁-Pro-Pro-R₆-Ser-R₈-Asp-Leu-R₁₁-D-Phe-His-R₁₄-Leu-Arg-Glu-R₁₈-Leu-R₂₀-Nle-R₂₂-R₂₃-Ala-R₂₅-Gln-Leu-Ala-R₂₉-Gln-Glu-R₃₂-R₃₃-R₃₄-Arg-R₃₆-R₃₇-Nle-R₃₉-R₄₀-R₄₁-NH₂ wherein Y₁ is an acyl group having not more than 7 carbon atoms; R₂₀ is Glu or D-Glu; R₂₂ is Ala or Thr; R₂₃ is Arg or Lys; R₂₉ is Gln or Glu; R₃₂ is His, ~~D-His~~, Aib or Ala; R₃₆ is Lys or Leu; R₃₇ is Leu or CML; R₃₉ is Glu or Asp; R₄₀ is Ile, CML or Glu; and R₄₁ is Ile, Aib or Ala; wherein the remaining variables are as defined in ~~claim 1~~ claim 15.

6. (currently amended) A peptide according to ~~claim 1~~ claim 15 wherein R₁₈ is Val, R₂₂ is Ala, R₂₃ is Arg, ~~R₂₄ is Ala~~, R₂₅ is Glu, ~~R₂₈ is Ala~~, R₃₉ is Glu, and R₄₁ is Ile.

7. (currently amended) A peptide according to ~~claim 1~~ claim 15 having the following formula, or a nontoxic salt thereof:

(cyclo 31-34)Y₁-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-R₂₂-R₂₃-Ala-Glu-Gln-R₂₇-Ala-Gln-Gln-Glu-R₃₂-R₃₃-Lys-Arg-Lys-Leu-Nle-Glu-R₄₀-Ile-NH₂ wherein Y₁ is an acyl group having not more than 7 carbon atoms; R₂₂ is Ala or Thr; R₂₃ is Arg or Lys; R₂₇ is Leu or CML; R₃₂ is His-~~or Aib~~; R₃₃ is Ser or Aib; and R₄₀ is Ile or CML.

8-10. (canceled)

11. (currently amended) A peptide ~~according to claim 1~~ having the formula:

(cyclo 31-34) Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle- Thr-Lys-Ala-Asp-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Asp-Ile- Ala-NH₂; or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys- Leu-Nle-Glu-Ile-Ile-NH₂; or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys- Leu-Nle-Glu-Ile-Ile-NH₂.

12. (currently amended) A peptide according to ~~claim 1~~ claim 13 having the formula:

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-CML-Arg-Glu-Val-Leu~~CML~~-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu- Nle-Glu-Ile-Ile-NH₂, or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-CML-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH₂; or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-D-Ser-Lys-Arg-Lys-Leu-Nle-Glu-CML-Ile-NH₂.

13. (currently amended) A 38-residue or 39-residue CRF ~~agonist~~ cyclic peptide, or a nontoxic salt thereof, which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula:
Y₁-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-R₁₄-R₁₅-Arg-R₁₇-R₁₈-R₁₉-Glu-Nle-Ala-Arg-Ala-Glu-Gln-R₂₇-Ala-Gln-Gln-Glu-R₃₂-R₃₃-Lys-Arg-R₃₆-R₃₇-Nle-Glu-R₄₀-R₄₁-NH₂
wherein Y₁ is an acyl group having not more than 15 carbon atoms or is radioiodinated tyrosine; R₁₄ is CML or Leu; R₁₅ is CML or Leu; R₁₇ is Glu or CML; R₁₈ is Val or CML; R₁₉ is CML or Leu; R₂₇ is CML or Leu; R₃₂ is ~~Aib~~, His or D-His; R₃₃ is Aib, D-Ala, D-Ser or Ser; R₃₆ is Lys or CML; R₃₇ is CML or Leu; R₄₀ is Ile or CML; and R₄₁ is Ile or CML; provided that a cyclizing bond exists between Glu in position 31 and Lys in position 34 and provided further that D-β-(2-naphthyl)alanine(D-2Nal) or D-Leu may be substituted for D-Phe.

14. (currently amended) A CRF agonist peptide, or a nontoxic salt thereof, which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula:
(cyclo 31-34) Y₁-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH₂, wherein Y₁ is an acyl group having not more than ~~15 carbon~~ than 7 carbon atoms or is radioiodinated tyrosine, and wherein a cyclizing bond may exist between the side chains of Glu in the 31-position and Lys in the 34-position.

15. (new) A 38-residue or 39-residue CRFR1 ligand cyclic peptide which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula, or a nontoxic salt thereof:
(cyclo 31-34)Y₁-Pro-Pro-R₆-Ser-R₈-Asp-Leu-R₁₁-D-Phe-His-R₁₄-R₁₅-Arg-Glu-R₁₈-Leu-R₂₀-Nle-R₂₂-R₂₃-Ala-R₂₅-Gln-R₂₇-Ala-R₂₉-Gln-Glu-R₃₂-R₃₃-R₃₄-Arg-R₃₆-R₃₇-Nle-R₃₉-R₄₀-R₄₁-NH₂ wherein Y₁ is an acyl group having not more than 7 carbon atoms or is radioiodinated tyrosine; R₆ is Ile, Met or Nle; R₈ is Leu or Ile; R₁₁ is Thr or Ser; R₁₄ is CML or Leu; R₁₅ is Leu or CML; R₁₈ is Val, CML, Nle or Met; R₂₀ is Glu or D-Glu; R₂₂ is Ala or Thr; R₂₃ is Arg or Lys; R₂₅ is Asp or Glu; R₂₇ is Leu or CML; R₂₉ is Gln or Glu; R₃₂ is His, Aib, Ala, Gly, Leu, Gln or Glu; R₃₃ is Aib or an L- or D-isomer of Ser, Asn, Leu, Ala, CML or Ile; R₃₄ is Lys or Orn; R₃₆ is Lys or Leu; R₃₇ is CML or Leu; R₃₉ is Glu or Asp; R₄₀ is Ile, CML or Glu; and R₄₁ is Ala, Aib or Ile; provided that D-β-(2-naphthyl)alanine(D-2Nal) or D-Leu may be substituted for D-Phe.